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MEDICATED WRAP

This is a continuation-in-part of U.S. Application Serial No. 09/561,170, filed April 27, 2000, which claims the benefit of U.S. Provisional Application Serial No. 60/131,857, which was filed April 29, 1999, the disclosures and contents of which are hereby incorporated by reference in their entireties.

1. Field of the Invention

The present invention relates to a medical device for relieving pain by simultaneously restricting movement of a body member, applying pain-relieving medicament, and applying pressure to acupuncture points.

2. Background of the Invention

Many people suffer from sprains, arthritis and other ailments at the joints such as the knees, elbows, wrists as well as neck pain. Often the treatment consists of wraps to stabilize and provide pressure to the joint, sports ointments and creams as well as prescribed and over-the-counter pain medications.

Many people suffering from such ailments are reluctant to take pain killing drugs over an extended period of time for fear of obtaining a dependency or simply based upon a general reluctance to take drugs. For these people, the remedies are limited to treatment through ice, heat, wraps and externally applied ointments such as sports creams and the like. The products such as wraps and ointments must be separately purchased. Further, the ointments and creams, if applied underneath a wrap, can stain and soil the wrap making it unsightly for the person to wear in public.

Still further, it is known that certain pressure joints near joints, if pressure is applied, can help to reduce and alleviate pain. The wraps and ointments heretofore used do not provide a means to impose an acupuncture effect to help reduce pain.

Thus there is a clear need in the art to overcome these drawbacks.

3. Summary of The Invention

The present invention relates to a device to be disposed around a body portion of a person for treating pain that body portion, wherein the device comprises a wrap having an interior surface for contacting the body portion, and adapted to be disposed around the body portion, said wrap being sufficiently elastic to enable the wrap to be stretched around the body portion to restrict the mobility of the body portion, at least one pad section secured to

contact predetermined areas of the injured member. The nodules are located strategically to provide acupressure-like force against specific acupressure points, which are well known in the art, thereby compressing the point and providing additional pain relief. See, for example, U.S. Patent Nos. 5,792,176, and 5,224,469, which disclose devices for the application of pressure ("acupressure") to selected points on the surface of the body which correspond to acupuncture points identified in Eastern medical practice.

The wrap has adjustable fastening means, such as VELCRO hook and loop fasteners, so that the user can stretch the wrap around the injured part and adjust the pressure so as to dispense medicament to the affected area and to select the desired pressure at the acupressure points.

Turning to the drawings, Fig. 1 shows a wrap 10 according to one embodiment of the present invention. The wrap 10 has an underside 12 adapted to be positioned against the skin when the wrap is used to treat a joint such as a knee or elbow or it can be of a size to wrap about the trunk of the body to treat the back. The wrap itself includes a main panel 14 connected to a side panel 16 by an elastic margin 18. At the end of the side panel 16 is one member 20 of a hook and pile fastener for securing the wrap 10 about the joint. Disposed on the body 14 is a pad 22 adapted to receive and store medicament for treatment of pain.

As shown in Fig. 3, if the pad 22 is loaded with the medicament by the manufacturer, a tearaway cover sheet 26 may be provided by which the user may tear away the protective cover to expose the pad 22 loaded with the medicament. The use of a tear-away cover is conventional technology.

The wrap 10 may also include one or more acupressure nodules 24 located to engage pressure points in the joint, muscle or ligament area to apply pressure thereto for the treatment of pain. As shown in Fig. 3, these nodules 24 may be spherical in shape and may be manufactured from a rigid product such as rubber, plastic or the like.

With reference to Fig. 2, at the top side 28 of the wrap 10 there is located the other member 30 for the hook and pile fastener for the wrap 10. Accordingly, and with reference to Fig. 4, the user would remove the protective strip or cover 26 to expose the pad 22 pre-loaded with medicament. The user would then place the pad 22 over, for example, the patella and position the wrap 10 about the knee joint securing it thereto using the members 20,30 of the hook and pile fastener. The elastic margin 18 enables the user to exert pressure by constricting or releasing the pressure imposed by the wrap 10 on the knee joint. In this position, as suggested in Fig. 4, the nodules 24 are disposed to the side and below the patella to exert acupressure effect on the ligaments of the knee joint.

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Turning to Figs. 5 and 6, a further embodiment of the wrap 10 for use at the wrist is shown. The wrap 10 includes the main panel 14 including the pad 22 to receive the medicament. A hole 32 is provided to pass the thumb when the wrap 10 is disposed about the wrist. Acupressure nodules 24 are provided to exert pressure at desired locations on the wrist. Straps 34a, b include the one member 20 of a hook and pile fastener, the other member 30 (not shown in Figs. 5 and 6) of the hook and pile fastener is disposed on the outside surface of the wrap 10.

Turning to Figs. 7-9, an embodiment of the wrap 10 for cervical use is disclosed. The wrap 10 includes the main panel 14 having the pad 22 to retain the medicament. Acupressure nodules 24 are provided to exert pressure at desired locations at the neck. The top side 28 includes the other member 30 of the hook and pile fastener. Straps 34a, b include the member 20 for the hook and pile fastener. Accordingly the wrap 10 is wrapped about the neck placing the pad 22 at the desired location to apply the medicament.

At least one nodule is provided on the interior of each wrap, and can be molded, sewn, welded, or otherwise secured to the interior surface of the wrap. The nodules are located on specific portions of the wrap in predetermined areas designed to correspond with known acupressure points for that specific body portion. These acupressure points as well-known and readily identifiable from medical literature, and may be adjacent areas of pain rather than directly on the pain. The nodules should be generally rigid, so that pressure can be applied quite specifically to the desired region of the member in which pain is being suffered. The nodules should have a generally curved surface, so as to not be pointed or have other sharp edges or protrusions that could injure the patient. The specific size of the nodule is not critical, although the area contacting the body should be sufficiently large so as to not create additional pain (e.g. by puncturing or sharply compressing the skin), but should not be so large as to distribute the pressure over a wider area than is necessary. Generally speaking, the area being compressed should be approximately 1/4-3/4 in diameter, depending on the specific area of the body involved. Examples of suitable nodules would be spherical lugs having diameter of 1/4-3/4 inch, preferably about 1/2 inch, though other shapes and dimensions may be usable depending upon the specific body part. For example, smaller nodules would be used for a wrist wrap, whereas larger nodules might be used for wraps for the knee or back. The nodules can be made from a generally rigid material such as hard rubber, but may have a small amount of resiliency (e.g. less than 10%) which could provide some patient comfort while not compromising the ability of the nodules to exert pressure.

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applied, the concentration of the active ingredient or ingredients of the applied medicament, and the nature of the vehicle, if any, containing the active ingredient or ingredients of the medicament. The nature of the vehicle selected is defined by, for example, the solubility of the active ingredient and/or active ingredients in the vehicle, rate of release of the active ingredient or active ingredients from the vehicle, the facility with which the vehicle hydrates the stratum corneum layer of the skin and thereby improves permeability of the skin barrier to the active ingredient and/or active ingredients, and the stability of the active ingredient and/or active ingredients in the vehicle. The choice of vehicle for dissolution or suspension of the active ingredient or ingredients is well known in the art (*See*, for example, Dirk B. Robinson and Howard I. Miabach, *Dermatologic Pharmacology* in BASIC AND CLINICAL PHARMACOLOGY, 871-87 (Bertram G. Katzung, Ed., Fifth Edition, 1992), which is hereby incorporated by reference in its entirety). The presence of one or more penetration enhancers, described below, in the medicament also affects the rate of diffusion of the one or more active ingredient of the medicament into and across the skin barrier.

The pad section may comprise, in various embodiments of the invention, one or more of the following elements: a backing film, a polymer matrix formulated with the active ingredient and/or a compartment filled with a vehicle comprising one or more active ingredients and, in certain embodiments, the vehicle may comprise one or more excipients, one or more membranes that control the rate of release of the active ingredient, pressure-sensitive adhesives that, in certain embodiments, comprise at least one active ingredient and may further comprise at least one excipient, an absorbent material such as, but not limited to, a cotton pad or a sponge, a protective, pressure-sensitive release liner, and a removable impervious cover element.

The backing film used in the pad section has an inner surface and an outer surface. The outer surface of the backing film is attached to the inner surface of the wrap. The composition of the backing film is selected according to, *inter alia* the nature of the active ingredient to be delivered and the length of time the wrap is to remain attached to the body. In certain embodiments, the backing film is constructed of a synthetic polyester to facilitate hydration of the outer surface of the skin. In other embodiments, the backing film is constructed of, as non-limiting examples, polyurethane or polyolefin polymers, and woven or non-woven fibrous materials such as cotton or polyesters and blends thereof. In certain embodiments, the backing film is the inner surface of the wrap.

The removable impervious cover element has an inner and outer surface. The edges of the inner surface of the cover element can be attached to the edges of the inner surface of the backing film, thereby forming a space within which the medicament is disposed. The

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Examples of suitable opioids for use with the invention as an active ingredient include, but are not limited to, alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, benzitramide, nor-binaltorphimine, bremazocine, buprenorphine, butorphanol, clonitazene, codeine, CTOP, DAMGO, desomorphine, dextromoramide, 5 dezocine, diampromide, dihydrocodeine, dihydrocodeine enol acetate, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, diprenorphine, DPDPE, eptazocine, ethoheptazine, ethylketocyclazocine, ethylmethylthiambutene, etonitazene, etorphine, fentanyl, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levorphanol, lofentanil, loperamide, 10 meperidine, meptazinol, metazocaine, methadone, metopon, morphine, myrophine, nalbuphine, naltrindole, benzoylhydrazone, naltrexone, narceine, nicomorphine, norlevorphanol, normethadone, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, papaverine, pentazocine, phenadoxone, phenazocine, phenoperidine, piminodine, pirtramide, proheptazine, promedol, propiram, propoxyphene, 15 remifentanil, spiradoline, sufentanil, tilidine, U50,488, and U69,593, amiphenazole, cyclazocine, levallorphan, nalmefene, nalorphine, naloxone, naltrexone, pharmaceutically acceptable salts thereof, and mixtures thereof.

Examples of peptide opioids that may be included in the medicament of the invention as an active ingredient include, but are not limited to, Tyr-Gly-Gly-Phe-Leu 20 ([Leu⁵]enkephalin), Tyr-Gly-Gly-Phe-Met ([Met⁵]enkephalin), Tyr-Gly-Gly-Phe-Leu-Arg-Arg-Ile-Arg-Pro-Lys-Leu-Lys-Trp-Asp-Asn-Gln (DynorphinA), Tyr-Gly-Gly-Phe-Leu-Arg-Arg-Gln-Phe-Lys-Val-Val-Thr (Dynorphin B), Tyr-Gly-Gly-Phe-Leu-Arg-Lys-Tyr-Pro-Lys (α -Neoendorphin), Tyr-Gly-Gly-Phe-Leu-Arg-Lys-Tyr-Pro (β -Neoendorphin), Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-Phe-Lys-Asn-Ala-Ile-Ile-Lys- 25 Asn-Ala-Tyr-Lys-Lys-Gly-Glu (β_h -Endorphin), [D-Ala²,MePhe⁴Gly(ol)⁵]enkephalin (DAMGO), [D-Pen²,D-Pen⁵]enkephalin (DPDPE), [D-Ser²,Leu⁵]enkephalin-Thr⁶ (DSLET), [D-Ala²,D-Leu⁵]enkephalin (DADL), D-Phe-Cys-Tyr-D-Trp-Orn-Thr-Pen-Thr-NH₂(CTOP), [D-Ala²,N-MePhe⁴,Met(O)⁵-ol]enkephalin (FK-33824), Tyr-D-Ala-Phe-Asp-Val-Val-Gly-NH₂ ([D-Ala²]Deltorphan 1), Tyr-D-Ala-Phe-Glu-Val-Val-Gly-NH₂ ([D-Ala²Glu⁴]Deltorphan 30 (Deltorphan II)), Tyr-Pro-Phe-Pro-NH₂ (Morphiceptin), Tyr-Pro-MePhe-D-Pro-NH₂ (PL-017), [D-Ala²,Leu⁵,Cys⁶]enkephalin (DALCE), pharmaceutically acceptable salts thereof, and mixtures thereof. Preferred opioids include morphine, loperamide and loperamide derivatives such as those disclosed in United States Patent Nos. 5,763,445; 5,981,513; 5,869,521; 5,744,458; 5,760,023; 5,798,093; 5,849,762; 5,811,078; 6,004,964; 5,962,477; 35 5,688,955; 5,888,494; 5,646,151; and 5,667,773 (all of which patents are incorporated by

reference herein, in their entirety), or pharmaceutically acceptable salts thereof, or mixtures thereof. The most preferred opioid is morphine or a pharmaceutically acceptable salt thereof. In certain embodiments the medicament comprises an opioid at a concentration of from about 0.01% to about 20%, from about 0.02% to about 15%, from about 0.05% to about 10%, from about 0.1% to about 5 %, and from about 0.5% to about 2.5%, by weight.

Excitatory neurotransmission is mediated in part by ligand-gated ion channels, and particularly by those cation channels activated by glutamate. There are at least three subtypes of such channels, which are named according to the preferred agonist of the associated receptor. One of these subtypes, accordingly, includes receptors referred to as the N-methyl-D-aspartate, or NMDA, receptors. A number of antagonists of NMDA receptors have been identified, including dizolcipine (MK-801), remacemide hydrochloride and its metabolites amantadine, budipine, and memantine, dextromethorphan and ketamine. Ketamine, dextromethorphan, and amantadine have been shown to alleviate chronic pain (Fisher *et al.* (2000), *J Pain Symptom Manage* 20 (5): 358-73, which is hereby incorporated by reference in its entirety), and ketamine has been shown to improve morphine analgesia (Mercadante *et al.* *J Pain Symptom Manage* (2000) 20 (4): 246-52, which is hereby incorporated by reference in its entirety).

Examples of suitable NMDA-receptor antagonists for use with the invention as an active ingredient include, but are not limited to, dextromethorphan, ketamine dizolcipine (MK-801), remacemide hydrochloride and its metabolites amantadine, budipine, memantine, and mixtures thereof. In certain embodiments of the present invention, the medicament comprises at least one NMDA-receptor antagonist and at least one opioid compound and/or at least one anti-cholinergic agent such as a tricyclic antidepressant, *e.g.*, amitriptyline (see for example, U.S. Patent No. 6,197,830, which is hereby incorporated by reference in its entirety). In certain embodiments the medicament comprises a NMDA receptor antagonist at a concentration of from about 0.25% to about 25%, from about 0.5% to about 15%, from about 1% to about 10%, and from about 2% to about 5%, by weight.

In another embodiment of the invention, the medicament further comprises at least one antiinflammatory corticosteroid as an active ingredient. Absorption of topically applied corticosteroid is enhanced significantly (up to 10 fold) using a plastic wrap, such as an impermeable backing film as used in certain embodiments of the present invention. (See, for example, Dirk B. Robinson and Howard I. Miabach, *Dermatologic Pharmacology* in *BASIC AND CLINICAL PHARMACOLOGY*, 871-87 (Bertram G. Katzung, Ed., Fifth Edition, 1992), which is hereby incorporated by reference in its entirety). Exemplary corticosteroids that

are suitable for use as an active ingredient in the medicaments of the present invention include, but are not limited to, the following (a typical, but non-limiting, concentration as weight %, is indicated for each): betamethasone dipropionate (0.05%), diflorasone diacetate (0.05%), halobetasol propionate (0.05%), amcinonide (0.1%), desoximetasone (0.25%),
 5 triamcinolone acetonide (0.5%), flucinolone acetonide (0.2%), diflorasone diacetate (0.05%), halcinonide (0.1%), flucinonide (0.05%), and mixtures thereof. In certain embodiments the medicament comprises a steroid or a corticosteroid at a concentration of from about 0.0001% to about 20%, from about 0.0005% to about 15%, from about 0.001% to about 10%, and from about 0.01% to about 5%, by weight.

10 The major pharmacological activity of tricyclic antidepressants is interference with serotonin and norepinephrine reuptake by neuron terminals. However, some tricyclic antidepressants have other pharmacological effects as well; that is, some tricyclic antidepressants not only relieve symptoms of depressive disorders, but also provide pain relief and muscle relaxation as well (*See Lane J. Wallace Psychopharmacological Agents*
 15 in REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY VOL II, 1180-95 (A. R. Gennaro, Ed. 19th Ed. 1995); Barkin *et al.* 2000, Am. J. Ther. 7(1): 31-47; and Lynch 2001, J. Psychiatry Neurosci. 26 (1): 30-36).

In certain embodiments of the present invention, the medicament comprises at least one tricyclic antidepressant, such as, but not limited to imipramine hydrochloride,
 20 imipramine pamoate, amitriptyline hydrochloride, amoxapine, desipramine hydrochloride, doxepin, protriptyline hydrochloride, trimipramine, and mixtures thereof, as an active ingredient. In another aspect of this embodiment, the serotonin (5-HT)-norepinephrine uptake inhibitor venlafaxine is also included as the, or one of the, active ingredients in the medicament of the present invention. In certain embodiments the medicament comprises a
 25 tricyclic antidepressant at a concentration of from about 0.01% to about 25%, from about 0.05% to about 15%, from about 0.1% to about 10%, and from about 0.5% to about 5%, by weight.

In certain embodiments of the present invention, the medicament comprises at least one excipient selected from the group consisting of preservatives, antioxidants,
 30 moisturizers, emollients, buffering agents, solubilizing agents, penetration enhancers, and skin protectants (*see, for example, (Monica Ramchandani and Rohinton Toddywala Formulation of Topical Drug Delivery Systems, in TRANSDERMAL AND TOPICAL DRUG DELIVERY SYSTEMS, 539-92 (Tapash K. Ghosh, William R. Pfister and Suil Yum, Eds. 1997, which is hereby incorporated by reference in its entirety).*

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(1% - 10%), sorbitan monooleate (1% - 10%), sorbitan monopalmitate, sorbitan monostearate (1% - 10%), and mixtures thereof.

In certain embodiments, the medicament comprises at least one permeation enhancer to facilitate or enable intradermal and transdermal delivery of one or more active ingredients of the medicament. Permeation enhancers generally chemically modify the skin in a manner that decreases the barrier properties thereof. Preferred permeation enhancers act rapidly and reversibly, are non-toxic, non-allergenic, non-irritating, and are pharmacologically inert (Tapash K. Ghosh and William R. Pfister *Transdermal and Topical Delivery Systems: An Overview and Future Trends*, in *TRANSDERMAL AND TOPICAL DRUG DELIVERY SYSTEMS*, 1-32 (Tapash K. Ghosh, William R. Pfister and Suil Yum, Eds. 1997, which is hereby incorporated by reference in its entirety). Suitable penetration enhancers for use in the invention and typical concentrations (expressed as w/w %) include, but are not limited to: propylene glycol (5% - 80%), alcohols (including ethanol and lauryl alcohol) (0.5% - 30%), esters such as glycerol monolaurate (1% - 10%), salicylic acid (1% - 5%), anionic surfactants such as sodium dodecyl sulfate (1% - 10%), cationic surfactants such as cetyltrimethyl ammonium bromide (1% - 10%), nonionic surfactants such as polysorbates (1% - 10%), phospholipids (1% - 10%), urea (1% - 5%), and mixtures thereof.

Suitable skin protectants for use in the invention and typical concentrations (expressed as w/w %) include, but are not limited to: allantoin (0.5% - 2%), dimethicone (1% - 30%), glycerin (20% - 45%), petrolatum (30% - 90%), zinc oxide (1% - 25%), and mixtures thereof.

In other embodiments of the present invention, the medicament comprises more than one active ingredient selected from, but not limited to, the following classes of compounds: opioids, corticosteroids, steroids, NSAID, local anesthetics, tricyclic antidepressants, and NMDA antagonists. In certain embodiments, the medicament comprises one of the following combinations of active ingredients: (a) an opioid and a NMDA antagonist; (b) an opioid and a local anesthetic; (c) a local anesthetic and a NMDA antagonist; (d) a tricyclic antidepressant and a NMDA antagonist. In a particular embodiment of the present invention, the medicament comprises a combination of amitriptyline and ketamine as the active ingredients.

The devices and methods of the present invention are used for the alleviation of pain in a body member by restriction of movement of the body member, application of pressure to acupuncture points, and the topical application of a suitable medicament. Accordingly, the methods and devices disclosed herein are used, in non-limiting examples, for the alleviation of pain in the toe, foot, ankle, calf, knee, thigh, hip, finger, knuckle, wrist,

forearm, elbow, upper arm, back, shoulder, and neck. Such pain may arise from, but not be limited to, arthritis, muscle strain, tendinitis, and repetitive motion syndromes including carpal tunnel syndrome.

5 The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention, in addition to those described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are intended to fall within the scope of the appended claims.

10 Various publications and patents are cited herein, the disclosures of which are incorporated by reference in their entireties.

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